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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/943,144	Applicant(s) KOSHIBA, TOMOKAZU	
	Examiner Russell Kallis	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09-14-01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The rejection under 35 U.S.C. 112, first paragraph new matter has been withdrawn in view of Applicant's arguments.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 18-30 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reasons of records set forth in the office action mailed 8/4/99, 4/25/00 and 6/7/01 and as stated below. Applicant's arguments filed 9/14/01 have been fully reconsidered but are not deemed persuasive.

The claims recite the limitation of a nucleotide sequence encoding an amino acid sequence of a 4.4Kbp gene obtainable from a plant, which is amplifiable with a combination of PCR primers from the group consisting of SEQ ID NO: 7, 8, 13, and 9-12, 14-15. Because no amplification conditions are specified, the claims read on any claimed nucleotide sequence of 4.4Kbp that encodes an aldehyde oxidase.

Applicant discloses a DNA sequence from maize that encodes an aldehyde oxidase, SEQ ID NO: 1 that is 4.4Kbp in length (actual length of the isolated clones as stated in the specification page 23 line 21 is 4.412Kbp, coding length is 4.074Kbp). Applicant does not

disclose other nucleotide sequences of 4.4Kbp length encoding aldehyde oxidase from plants, and hence Applicant has not adequately described the genus of sequences encoding an aldehyde oxidase from plants that are 4.4Kbp in length and are isolated by PCR using the primers of SEQ ID NO: 7-15.

Whereas the specification describes another aldehyde oxidase clone from maize, SEQ ID NO: 3, the nucleotide sequence is 4.359Kbp in length, not 4.4Kbp. In addition, the coding region for this clone is 4.047Kbp encoding an enzyme of different size than that encoded by the 4.4Kbp clone of which the entire coding sequence is 4.205Kbp. Moreover, Applicant has not described any structural properties of aldehyde oxidase nucleotide sequences that are distinctive of the genus.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining a cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

3. Claims 18-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a 4.4Kbp aldehyde oxidase nucleotide sequence of SEQ ID NO: 1, does

not reasonably provide enablement for any aldehyde oxidase nucleotide sequence from any plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant claims an isolated polynucleotide encoding an aldehyde oxidase enzyme, a plasmid comprising a polynucleotide encoding an aldehyde oxidase enzyme wherein the cloned nucleotide sequence is 4.4Kbp in length and amplifiable from a plant using PCR primers specific to said sequence, host cells and plants transformed with an expression vector operable in plants, and a method of controlling aldehyde oxidase expression in plants.

Applicant teaches isolation of 4.412Kbp (SEQ ID NO: 1) and 4.359Kbp (SEQ ID NO: 3) maize aldehyde oxidase clones using maize mRNA as template in a RT-PCR reaction (Example 8), primers specific to the amplified maize aldehyde oxidase cDNA for use in a RACE PCR reaction (Example 8), and the cloning of the products into a plasmid to make a complete open reading frame of a maize aldehyde oxidase cDNA (Example 7), the construction of an expression plasmid comprising the amplified maize aldehyde oxidase cDNA, a promoter, and a terminator operable in a plant cell and plant. (Examples 10-11), and transformation of plants (Examples 12-13).

Applicant does not teach the isolation of any 4.4KBP aldehyde oxidase gene other than maize aldehyde oxidase of SEQ ID NO: 1 and modified aldehyde oxidase expression in a plant transformed with an aldehyde oxidase cDNA.

It is well known in the art that plant DNA coding sequences diverge with respect to sequence identity and that unpredictability in isolating cDNA sequences using PCR techniques requires testing and optimizing the various reaction parameters. This view is supported by the Marathon PCR manual by Clontech. In section XVI first paragraph, the manual states in no ambiguous terms, "It is generally advisable -and often necessary- to optimize your 5' and 3' RACE reactions. This generally consists of improving the yield of your desired fragments, while decreasing the amount of background or nonspecific and/or incomplete bands in your RACE reactions.". Furthermore, the amount of gene product activity required to accelerate developmental processes to an advantageous degree is unknown and the mechanism by which plant hormones is not well understood. The unpredictability in metabolic engineering arises from a lack of understanding of the complex interactions of both regulation and coordination of metabolism and the potential for perturbation of these processes that may arise when engineered changes to metabolic pathways introduce novel interactions (De Luca, V., Ag Biotech News and Information. 1993 Vol. 5, No. 6, pp. 225N-229N) (page 225N, column 2, lines 6-8). The unpredictability is exemplified in the overexpression of jasmonic acid in transgenic tobacco that did not have the expected effect of altering the phenomenology of the preexisting wild type wound response mechanism (Harms *et al.* The Plant Cell, Vol. 7, pp. 1645-1654, October 1995) (page 1646, column 1, lines 13-29). The unpredictability inherent in modifying gene expression levels would require further experimentation for one of skill in the art.

Because the specification provides no guidance for amplifying aldehyde oxidase using the maize PCR primers of SEQ ID NO: 7-15 from species other than maize or for using PCR primers comprising conserved regions of the aldehyde oxidase cDNA one of skill in the art

would be required to optimize PCR conditions to eliminate non specific binding and the artifacts generated thereof. This would comprise adjustments in annealing temperatures, testing different concentrations of Mg and template, and the sequencing of putative clones for each species of aldehyde oxidase cDNA amplified to verify the product as aldehyde oxidase. The unpredictability in the art would require screening numerous transgenic plants to test various constructs for effectively modified levels of aldehyde oxidase presuming they could ever be obtained.

Given the lack of guidance, the absence of several working examples in the specification that reflect the breadth of the claims, and the unpredictability in the art, undue trail and error would be needed to practice the invention. Therefore, the invention is not enabled.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 18, 20-22, and 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claims 18, 22, and 26-28 section (e), lines 1-2, the claim recites "a nucleotide sequence encoding an amino acid sequence of a 4.4Kbp gene obtainable from a plant, which is amplifiable". It is unclear if it is the "nucleotide sequence" or "the 4.4Kbp gene" that is amplifiable. The claim should read, --a nucleotide sequence of a 4.4Kbp gene encoding an amino acid sequence, wherein said 4.4Kbp gene is amplifiable--.

At Claims 18 and 22, line 3, and at Claim 26 line 6, Claim 27 line 5, and Claim 28 line 8, the claims recite "and having a nucleotide sequence selected from the group consisting of " is

unclear and should read --and wherein said polynucleotide has a sequence selected from the group consisting of--.

At Claims 20 and 21, line 2, the claims recites "The isolated polynucleotide. . .", "which is derived from maize plant". The use of the term derived is unclear and suggests that the isolated polynucleotide was changed in the process and is no longer the same as the endogenous maize gene.

At Claim 21, line 2, the claim recites "(Zea mays". The claim should recite (Zea mays L)

At Claim 25, line 2, the claim recites "wherein the host cell is a plant". It is not clear since plants are multicellular organisms. A plant is not a cell.

At Claim 26, line 3, the beginning of the second limitation "(2) a polynucleotide. . ." should begin on a new line and should be indented.

At Claim 26, line 3 and 20, Claim 27, lines 2 and 20, and Claim 28, line 5 and 23, the use of the term "capable of functioning" is unclear because it is not stated whether the described components function or not.

At Claim 26, lines 20-21, the claim recites "in a functional manner and in the order described above". This part of the claim should be recited at the beginning of the claim. The beginning of the claim should read --A process of constructing an expression plasmid which comprises ligating in a functional manner and in the order described:--

At Claim 28, lines 20-21, the claim recites "in a functional manner and in the order described above to transform said host cell". The claim should recite at the end of the claim, --wherein the aldehyde oxidase of the transformed host is controlled--.

At Claim 28, line 1, use of the term "controlling production" is unclear because it is not known whether production is controlled in amount, location, time, or some other way.

Response to Arguments

Applicant's arguments filed September 14, 2001 have been fully considered but they are not persuasive. Applicant asserts that the specification sufficiently describes structural attributes that are common to members of the polynucleotide genus that distinguish the polynucleotide genus (that encode plant aldehyde oxidases), that members of the genus have a 4.4Kbp structural attribute and are amplifiable with primers from group consisting of SEQ ID NO: 7-15. It is further stated in the response file September 14, 2001 that the Office Action has not set forth reasons why there is insufficient written description of the polynucleotide genus. Applicant also states the rejection is based upon a misconception that the polynucleotide recited in (e) of Claim 18 encompasses "all plant aldehyde oxidase". (response, p. 7-8)

Applicant further argues that it is unnecessary to describe *haec verba* the parameters for the amplification, since one of ordinary skill in the art can certainly determine from the information provided in the specification, the parameters thereof. (response, p. 9)

First, the specification does not describe any other members of the polynucleotide genus, only one, SEQ ID NO: 1. To satisfy the written description requirement Applicant must describe members of a genus (i.e. more than one) that have structural features common to the members of the genus and not describe a structural feature from one candidate gene and then postulate *a priori* that there are others in existence somewhere else in the plant kingdom. Second, the property of being amplifiable with primers from the groups consisting of SEQ ID NO: 7-8,13 and SEQ ID NO: 9-12,14-15 is not a structural property of the polynucleotide genus. It is well

know to one of average skill in the art that under different PCR conditions those primers would amplify DNA sequences other than SEQ ID NO: 1 that encode proteins other than an aldehyde oxidase. Since non aldehyde oxidase DNA can be amplified by the said primers they alone do not constitute a structural property of the genus. Furthermore, the written description requirement does not recognize the functional description of a gene as an adequate description because this is a description of what the gene does and not what it is.

Applicant further argues that the rejection is based on a misconception that the polynucleotide recited in (e) of Claim 18 encompasses "all plant aldehyde oxidase" (response p. 10-11). Because no PCR reaction conditions are recited in claim 18(e), the claim does not encompass all plant aldehyde oxidase nucleotide sequences. The written description requirement is clear in its demand upon Applicant to describe member sequences of the genus that encode plant aldehyde oxidase.

11. All claims remain rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 308-0009.

Russell Kallis Ph.D.
May 30, 2002

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